The mechanical behavior of soft, hydrated biological tissues

Ever wonder what the elastic modulus of your skin was? Probably not, but the mechanical response of biological material does hold keen interest for those diagnosing disease-related degeneration of tissues, as well as those designing prosthetics, body armor and drug delivery systems. Murat Okandan (1749), who is developing silicon MEMS-based retinal replacements, and ophthalmologist Stephan McLeod (University of California, San Francisco), who is putting into practice hard plastic implantable lens replacements, are two researchers who want to know exactly how tissue behaves. As they have found, engineering biocompatibility in devices that interface with the human body is challenging since most engineered materials do not behave like living ones. Soft tissues have a unique combination of toughness and suppleness, and can deform dramatically before accumulating significant stresses. By investigating the mechanics of this behavior, the Laboratory Directed Research and Development team of Brad Boyce (1824), Vicky Nguyen (8776) and Reese Jones (8776), with the help of technician Mark Grazier (1824) and viscoelasticity expert Bob Chambers (1523), hope their research will guide the development of unique biomimetic materials as well as provide insights into the biocompatibitity problem.

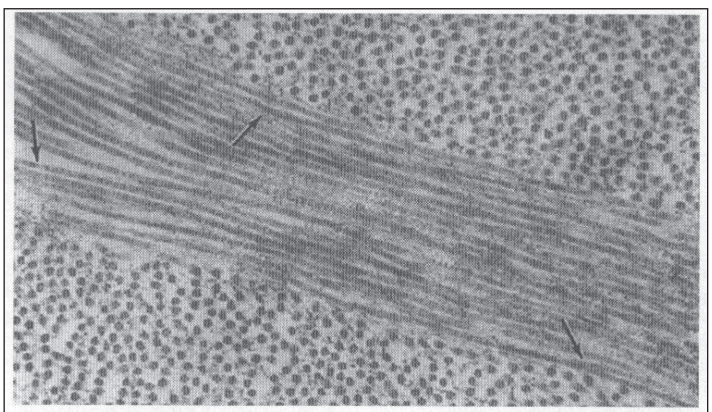


Figure 1: Cross-section of stroma (Adler)

The team selected corneal tissue, the transparent layer in front of the lens, as the target material since it is like a simplified and very structured type of skin. It is simplified in the sense that the cornea is avascular and lacks many of the other non-structural components of ordinary skin. The structure of the interior of the cornea is shown in Figure 1. The black dots and lines in the micrograph are (type I) collagen fibrils, while the white interstitial matter is composed largely of water, the polysaccharide proteoglycan and protein. The collagen is arranged in lamella of parallel fibrils that are stacked at oblique angles from the posterior of the cornea to the anterior and are bound by the hydrated proteogylcan matrix. The fibrils are evenly spaced, allowing the cornea to be transparent. (In fact, the specific spacing is tuned to minimize destructive interference and the mild swelling that occurs after extraction is enough to make the cornea occlude.) From an engineering perspective, the cornea has aspects of a solid-fluid mixture and a fiber-reinforced composite, which is a combination rarely found in engineered materials.

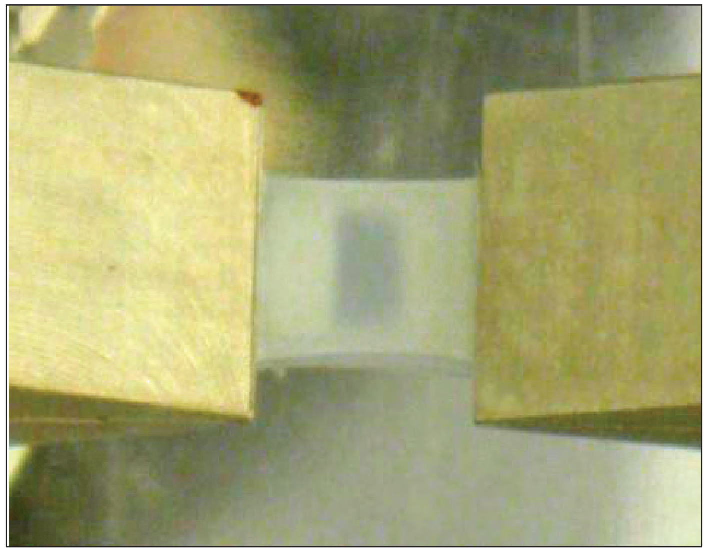


Figure 2: Corneal tension strip

The mechanical difference between preserved tissue and fresh is as striking as that between a cooked egg and a raw one. To replicate the in vivo constitution as closely as possible, the team found sources for bovine eyes that were harvested immediately after slaughter. Other complications beyond those normally encountered in material testing were biosafety regulations, the need for pneumatic grips to hold the slippery yet delicate tissue and, of course, the actual extraction and preparation of samples for tension testing. Figure 2, which is not in sharp focus due to a hydration bath, shows a uniaxial tensile sample under stress. Particular care was given to pre-conditioning the tissue with repeated stress cycles designed to obtain an entirely recoverable deformation and repeatable measurements. This procedure, which is unnecessary for most engineered materials, allows for any incipient reconfiguration after excision to take place. Another challenge with testing tissues is that they exhibit large natural variation in properties. To characterize this inherent variability between samples from different individuals (and sometimes even from right-left pairs) all tests were performed on sample sizes on the order of 10.

Creep and constant-rate experiments were performed to quantify the mechanical response of the tension strips. In a creep test the stress level is held constant and the stretch is measured over time. In the constant-rate tests, stress is ramped up, held and then ramped down. The results of these experiments are shown in Figures 3 and 4, which illustrate the distinctly non-linear time-dependent mechanical response of the cornea.

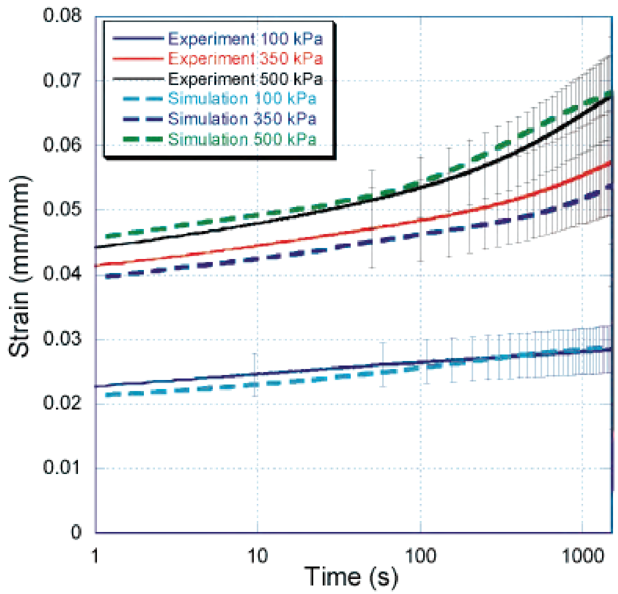


Figure 3: Creep strain

These curves are characteristic of a viscoelastic material, which was modeled with a free energy density and stress response that is the sum of an equilibrium and a time-evolving non-equilibrium part. Given the apparent structure of the cornea, the stress response was further divided into the sum of an isotropic matrix and an anisotropic component due to the fibrils. Because it was not possible to measure the properties of the soft hydrated matrix independently from the current tests, the matrix was assumed to be incompressible, weak and relatively inviscid compared to the fibril network and could be adequately represented by a neo-Hookean hyperelastic model. A phenomenological approach was also used to describe the behavior of the fibril network. To reproduce the J-shape stress-strain curves obtained in experiments (see Figure 4), the statistical average of a large number of fibers, each with an exponential rise of tension with stretch, was employed. Since the creep response in Figure 3 is obviously stress dependent (i.e., the lower stress level is insufficient to engage the mechanisms seen at the two higher stress levels), it was necessary to introduce a viscosity dependent on an activation stress. This viscosity controls the rate of evolution of the non-equilibrium component of the stress and at higher stress levels decreases, as the activation switch turns on, to exhibit increased stretch. To obtain the simulated response shown in Figures 3 and 4, the model was fitted to the creep response for the high and low loads and to the loading part of the high load constant-rate. The predicted creep response at the medium load and the two lower load stress-strain curves compares well with the corresponding experiments, by displaying representative trends that are well within the material variability.

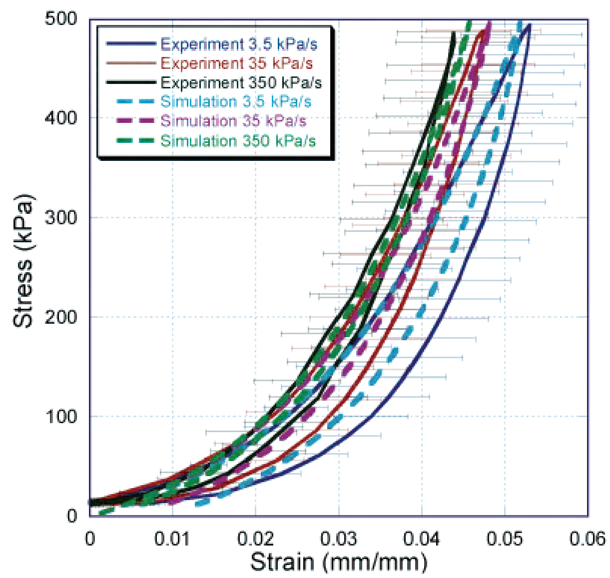
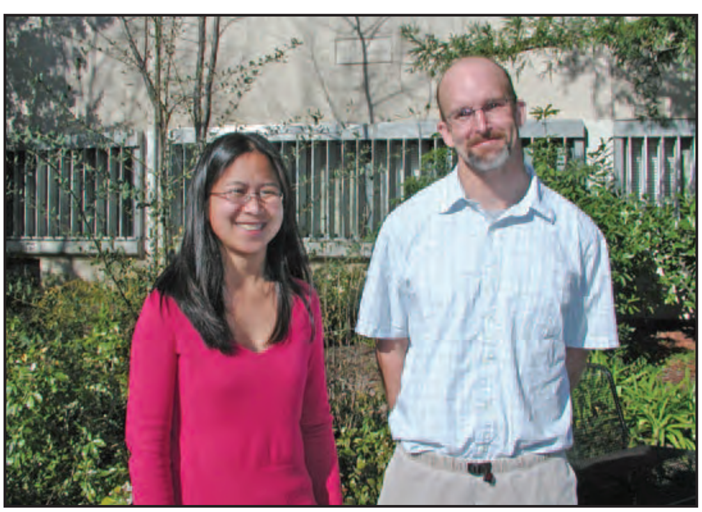


Figure 4: Stress-strain cycles

The team is currently working on in-plane compression experiments to characterize the matrix response, constructing explicit models of the fibril-matrix structure to investigate their interaction and developing its collaborations in the medical arena.



Vicky Nguyen, left, obtained her PhD from Stanford University in 2004, and joined Dept. 8776 that same year. Her research interests are modeling the inelastic behavior of materials, including their fracture and failure. Reese Jones, right, received his PhD in 1998 from the University of California, Berkeley and came to Sandia that year. He works in Dept. 8776 on computational mechanics, biomechanics, molecular dynamics and optimization. Their fellow team member, Brad Boyce (1824), joined Sandia in 2001 after receiving his PhD that year from the University of California, Berkeley. His research interests include mechanical reliability, fracture, and fatigue of structural materials.